

AMENDMENTS TO THE CLAIMS

1. (Original) A microwell array chip that has multiple microwells and is employed to contain a single lymphocyte specimen in each microwell and detect antigen-specific lymphocytes in single units; wherein the microwell array chip is of a shape and of dimensions where only one lymphocyte is contained in each microwell.
2. (Original) The microwell array chip of claim 1, wherein the microwell is of cylindrical, rectangular parallelepiped, inverse conical, or inverse pyramid shape, or some combination of two or more thereof.
3. (Currently amended) The microwell array chip of claim 1 ~~or~~ 2, wherein the diameter of the maximum circle inscribable in a planar configuration of the microwells falls within a range of from one to two times the diameter of the lymphocytes that are to be contained in the microwells, and the depth of the microwells falls within a range of from one to two times the diameter of the lymphocytes to be contained in the microwells.
4. (Original) A microwell array chip that is employed to detect antigen-specific lymphocytes and has multiple microwells each containing a single lymphocyte specimen.
5. (Original) The microwell array chip of claim 4, wherein the microwell has a diameter of from 5 to 100 micrometers and a depth of from 5 to 100 micrometers.

6. (Currently amended) The microwell array chip of claim 4 ~~or 5~~, wherein the lymphocyte specimen is contained in the microwell together with a culture medium.
7. (Currently amended) The microwell array chip of ~~anyone of claims 4 to 6~~ claim 4, wherein the lymphocyte specimen is derived from blood.
8. (Currently amended) The microwell array chip of ~~anyone of claims 4 to 7~~ claim 4, wherein the lymphocyte specimen is a B lymphocyte or T lymphocyte.
9. (Currently amended) A method of detecting antigen-specific lymphocytes comprising the steps of adding antigen to each microwell in the microwell array chip according to ~~anyone of claims 4 to 8~~ claim 4, stimulating the lymphocyte specimen, and detecting lymphocyte specimens reacting with the antigen.
10. (Original) The method of claim 9, wherein the detection of cells reacting with antigen is conducted by using Ca ion dependent fluorescent dye.
11. (Original) The method of claim 9, wherein the detection of cells reacting with antigen is conducted by employing, as a marker, an activated marker protein expressed on the surface of the activated lymphocyte specimen that has been stimulated with antigen.

12. (Original) The method of claim 9, wherein the detection of cells reacting with antigen is conducted by employing, as an indicator, the degree of polarization of fluorescence emitted by a fluorescent substance in the lymphocyte specimen.

13. (Original) The method of claim 9, wherein the detection of cells reacting with antigen is conducted by employing, as an indicator, the proliferation of the lymphocyte specimen or the production of antibody.

14. (Currently amended) The method of ~~anyone of claims 9 to 13~~ claim 9, wherein the antigen is a protein, peptide, DNA, RNA, lipid, sugar chain, or organic macromolecular compound.

15. (Currently amended) The method of ~~anyone of claims 9 to 13~~ claim 9, wherein the antigen is a bacterium, virus, autoantigen, tumor antigen, or allergen.

16. (Currently amended) A method of manufacturing antigen-specific lymphocytes comprising the step of recovering from microwells lymphocyte specimens reacting with antigen that have been detected by the method of ~~anyone of claims 9 to 15~~ claim 9.

17. (Original) A method in which a single lymphocyte reacting specifically with a certain antigen (referred to hereinafter as an antigen-specific lymphocyte) is selected and an antigen-specific antigen receptor gene is cloned from the single antigen-specific lymphocyte.

18. (Original) The method of claim 17, wherein the selection of the antigen-specific single lymphocyte is conducted by adding antigen to each microwell in an antigen-specific lymphocyte detection-use microwell array chip having multiple microwells each containing a single lymphocyte specimen, detecting which lymphocytes have reacted with the antigen, and removing the antigen-specific lymphocytes that have been detected from the microwells.
19. (Original) The method of claim 17, wherein the antigen-specific lymphocyte is present in a frequency of 0.1 percent or less.
20. (Currently amended) The method of ~~anyone of claims 17 to 19~~ claim 17, wherein the antigen-specific lymphocyte is broken down using a cytolytic agent and the antigen-specific antigen receptor gene is amplified by RT-PCR.
21. (Original) The method of claim 20, wherein the RT-PCR is conducted by preparing cDNA with reverse transcriptase and carrying out PCR twice with primer mixes for antigen receptor gene.
22. (Currently amended) The method of ~~anyone of claims 17 to 21~~ claim 17, wherein the antigen-specific lymphocyte is a B lymphocyte or T lymphocyte.

23. (Original) The method of claim 22, wherein the antigen-specific antigen receptor gene is an immunoglobulin gene when the antigen-specific lymphocyte is a B lymphocyte, and a T-cell receptor gene when the antigen-specific lymphocyte is a T lymphocyte.

24. (Currently amended) The method of ~~anyone of claims 17 to 23~~ claim 17, wherein the antigen-specific lymphocyte is a B lymphocyte and an antigen-specific immunoglobulin gene is cloned.

25. (Currently amended) The method of ~~anyone of claims 17 to 23~~ claim 17, wherein the antigen-specific lymphocyte is a T lymphocyte and an antigen-specific T-cell receptor gene is cloned.

26. (Currently amended) The method of ~~anyone claims 18 to 25~~ claim 18, wherein gene amplification is conducted in the microwell without removing from the microwell the antigen-specific lymphocyte that has been detected.

27. (Original) A method of manufacturing monoclonal antibody using the antigen-specific immunoglobulin gene that has been cloned by a method of claim 24.

28. (Original) A method of manufacturing material for gene therapy employing the antigen-specific T-cell receptor gene that has been cloned by a method of claim 25.